UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/546,573	04/10/2000	Mads Holten-Andersen	19829-000300US	3408

7590 07/02/2002

STANISLAUS AKSMAN, ESQ
HUNTON & WILLIAMS
1900 K STREET NW SUITE 1200
WASHINGTON, DC 20006

EXAMINER	
RAWLINGS, STEPHEN L	

ART UNIT	PAPER NUMBER
1642	17

DATE MAILED: 07/02/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Acti n Summary	Applicati n No. 09/546,573	Applicant(s) HOLTEN-ANDERSEN ET AL.	
	Examiner Stephen L. Rawlings, Ph.D.	Art Unit 1642	

-- The MAILING DATE of this communication appears on the cover sheet with the c rrespondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 March 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-15,18-36 and 38-40* is/are pending in the application.

4a) Of the above claim(s) *6-12 and 20-26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4,5,13-15,18,19,27-36 and 38-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1,4-15,18-36 and 38-40* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. The amendment filed March 11, 2002 in Paper No. 16 is acknowledged and has been entered in part. Claims 2, 3, 16, 17, and 37 have been canceled. Claims 1, 4, 13-15, 18, 27, 28, 30, 34, and 37 have been amended. Claims 38-40 have been added.

2. Claims 1, 4-15, 18-36, and 38-40 are pending in the application. Claims 6-12 and 20-26 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a non-elected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 7.

3. Claims 1, 4, 5, 13-15, 18, 19, 27-36, and 38-40 are currently under prosecution.

Specification

4. In the previous Office Action mailed November 9, 2001 (Paper No. 10), the abstract of the disclosure was objected to because its placement in the specification is improper. In Paper No. 16 Applicants sought to properly place the abstract; however, because the abstract was not printed on a separate appropriately numbered page, the amendment was not entered. In reply to this Office Action, Applicants are required to submit a separate page containing the abstract with a request that the page be properly placed and entered.

Claim Objections Withdrawn

5. Claims 4, 5, 13, 14, 18, 19, and 27-37 have been amended to render the ground of objection to the claims moot. Accordingly, claims 4, 5, 13, 14, 18, 19, and 27-37 are treated on the merits in this Office Action.

Grounds of Claim Rejections Withdrawn

6. In the previous Office Action, claims 1-3 and 15-17 were rejected under 35 USC § 112, second paragraph. Unless specifically reiterated below, Applicants' amendment has obviated the grounds of rejection stated in the previous Office Action, or alternatively, Applicants' arguments were persuasive and have been favorably considered.

Grounds of Claim Rejections Maintained and Response to Applicants' Remarks
Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1, 4, 5, 13-15, 18, 19, 27-36, and 38-40 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention for the reasons set forth in the previous Office Action mailed November 9, 2001 (Paper No. 10).

Presently, claims 1, 4, 5, 13, 14, 30-36, and 38-40 are drawn to a method for determining whether an individual is likely to have gastrointestinal cancer. Claims 15, 18, 19, 27, and 30-36 are drawn to a method for determining whether a patient who has been treated for primary breast cancer is likely to have metastatic breast cancer.

In brief summary of the grounds of rejection, the specification fails to meet the enablement requirement set forth under 35 USC § 112, first paragraph because the amount of guidance, direction, and exemplification disclosed in the specification is insufficient to enable the skilled artisan to make and/or use the claimed invention with a reasonable expectation of success without having need to perform additional, undue experimentation. Factors to be considered in determining whether undue experimentation is required are summarized in *Ex parte Forman*, 230 USPQ 546 (BPAI 1986). They include the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the

specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed.

Applicants have traversed these grounds of rejection arguing that use of the claimed invention is sufficiently enabled by Applicants' disclosure to meet the requirements set forth under 35 USC § 112, first paragraph. In particular, Applicants have argued there is no legal precedent that requires Applicants to submit experimental data to verify that their invention is operable, but nonetheless Applicants have asserted that the use of the claimed invention to determine the likelihood that an individual or a patient has or will have primary colorectal cancer or metastatic breast cancer has been demonstrated in the specification. Furthermore, Applicants have argued that the claimed invention is not directed to a single, precise value of a TIMP-1 concentration that enables the skilled artisan to discriminate a patient or individual having, or who will have cancer, because the discriminating value may be arbitrarily determined by the practitioner, depending upon the desired level of specificity and selectively. Applicants have noted that should the practitioner practice the method using a discriminating value that provides relatively low specificity, the method will tend to produce false positive results. On the other hand, should the practitioner practice the method using a discriminating value that provides relatively low sensitivity, Applicants have remarked that the method can be used with a relatively greater certainty that only patients or individual having, or who will have malignant colorectal cancer will be identified. In addition, with regard to PSA, Applicants have further remarked that although there is not a consensus as to what threshold, or discriminating value, should be used, the marker is nonetheless widely used. Since the Office Action states that given only the benefit of Applicants' disclosure, the skilled artisan would not accept the assertion that measuring the concentration of TIMP-1 alone can be used as a reliable diagnostic marker, Applicants have contended the invention and experimental results disclosed in Applicants' specification are "truly novel, unobvious and enabled to a person skilled in the art" (page 9, paragraph 1). Applicants have also asserted that the standard that has apparently been applied to Applicants' specification to determine whether the disclosure

is enabling contradicts the standard used by the courts, and have further asserted that the standard used by the Office "would substantially correspond to a standard necessary for an FDA approval" (page 11, paragraph 2). Applicants have remarked that the scientific community has expressed significant interest in their invention, which Applicants contend rebuts the statement that the skilled artisan would not accept the assertion that the claimed invention can be used to diagnose any type of cancer, including colorectal and breast cancer. Finally, Applicants argue that the Examiner used a statement published by Applicants, which suggested the need to perform further studies to validate the clinical usefulness of measuring TIMP-1 concentrations, out of context, as Applicants assert that statement "is related to prognosis and has nothing to do with diagnosis" (page 11, paragraph 4).

In reply to Applicants' arguments, there is no factual evidence disclosed in the specification that would lead the skilled artisan to reasonably conclude that the concentrations of TIMP-1 in a bodily fluids of patients correlates positively with the presence, or the probable incidence of cancer in those patients. Furthermore, given only the benefit of Applicants' disclosure, the skilled artisan, in practicing the claimed method using the disclosed median value of the concentration of TIMP-1 in individual having colorectal cancer, would conclude that a significant number of healthy, disease-free individuals had colorectal cancer. Because the range of the values of the concentrations of TIMP-1 in the bodily fluid of patients known to have cancer substantially overlaps the range of the values of the concentrations of TIMP-1 in the bodily fluid of individuals considered healthy and disease-free, the discriminatory value of the concentration of TIMP-1 in the bodily fluids, which might delineate one group from the other, is obscured. For example, the values of the concentration of TIMP-1 in patients previously diagnosed with colorectal cancer are disclosed as ranging from 53.7 to 788.7 micrograms/liter, but the values of the concentration of TIMP-1 in disease-free individuals are disclosed as ranging from 51.0 to 156.2 micrograms/liter. The substantial overlap in the ranges of the values of the TIMP-1 concentrations in the plasma of affected and unaffected individuals underscores a lack of predictability. As noted in the previous Office Action, Oberg, et al also observed similarly wide,

overlapping ranges of concentrations. Evidence of such a large overlap, in further view of the teachings of Michael, et al, Ikebe, et al, Jung, et al, McKay, et al, Aoudjit, et al, and Berend, et al, supports the conclusion that in the absence of working exemplification, the skilled artisan would not have a reasonable expectation of successfully practicing the claimed invention without the need to perform additional, undue experimentation.

Moreover, according to the teachings of Tockman, et al, the diagnostic utility of any biomarker should first be validated before it should be used as a basis for determining that an individual has cancer. Applicants' have not established a statistically significant correlation of the value of the concentration of TIMP-1 in an individual's plasma or urine and the presence or incidence of colorectal cancer to show that the claimed method can be used to predictably determine whether or not an individual having a particular concentration of TIMP-1 in his or her plasma or serum has or will have colorectal cancer; and therefore it does not appear that Applicants have validated the diagnostic utility of their proposed biomarker. As the claimed methods have not been exemplified in Applicants' disclosure, there is no factual evidence supporting Applicants' assertion that the claimed methods can be used successfully to determine the likelihood that an individual or a patient has, or will have primary colorectal cancer or metastatic breast cancer. Considering the Forman factors, which are summarized above, the preponderance of evidence supports the conclusion that Applicants' disclosure would be insufficient to enable the skilled artisan to practice the claimed methods with a reasonable expectation of success without the need to first perform additional, undue experimentation.

Nonetheless, Applicants have argued that the threshold value, which can be used to discriminate between an individual having cancer from an individual not having cancer, is arbitrary. Depending upon the desired degree of specificity and sensitivity, the skilled artisan can choose the discriminating value to be used in practicing the claimed methods. The claims are drawn to a method for determining whether an individual is *likely* to have or will have gastrointestinal cancer or metastatic breast cancer, but unless the method can be used with a high degree of predictability to

determine whether or not the individual does, in fact, have or will have cancer, it is not apparent that the claimed method would have a specific and substantial utility. Applicants have asserted that the invention can be used to screen large populations for the occurrence of cancer and therefore Applicants have disclosed that the invention provides a "highly specific" method for identification of patients having cancer. However, as noted above, the specification fails to disclose a discriminatory value of the concentration of TIMP-1, which would enable the invention to be used with such a high degree of specificity. Accordingly, the skilled artisan would necessarily have to first determine which discriminating value should be used to have a reasonable expectation of success in practicing the claimed method to screen members of a population and identify individuals having, or at risk for having cancer. In other words, to have a reasonable expectation of successfully determining whether an individual has or will have cancer, the practitioner of the claimed method will need to use a threshold value that most assuredly reveals the presence of cancer in the individual, but since the specification does not teach which value or values can be used in practicing the claimed methods to accomplish the objectives recited in the preamble of claims 1 and 15, the skilled artisan would first need to determine the discriminatory value of the threshold that will provide the required specificity. Moreover, one skilled in the art would necessarily have to first validate the threshold value by determining that the method can be used reliably and accurately.

Again, the specification fails to demonstrate that the level of TIMP-1 in a bodily fluid of an individual positively correlates with the probability of finding gastrointestinal cancer, or alternatively correlates an increased risk for developing metastases of a primary breast cancer. As Applicants have noted in their remarks, even the utility of widely used markers, such as PSA has been called into question, as there is not a consensus in the art establishing the utility of PSA as a diagnostic or prognostic marker. In fact, the scientific community continues to debate the value of PSA and many other markers, but accordingly it seems that the wide use of PSA as a marker cannot be considered to constitute evidence that TIMP-1 can be used as a marker in practicing the claimed invention.

The standard used to determine whether or not Applicants' disclosure meets the enablement requirement set forth under 35 USC § 112, first paragraph is not inconsistent with the standard used by the courts, nor is it the same as that used by the FDA. Applicants are not required to secure FDA approval to establish the patentability of a claimed invention, only to demonstrate that given only the benefit of Applicants' disclosure, the skilled artisan would have a reasonable expectation of successfully using the claimed invention to determine, for example, whether an individual treated previously for a primary breast cancer is likely to have or to develop metastases thereof without the need to first perform additional, undue experimentation. As to whether undue experimentation would first need to be performed, the standard that has been used is the same as that used by the courts, namely a weighing of factual evidence using the Forman factors.

Accordingly, Applicants' arguments have been carefully considered but in view of the preponderance of evidence have not been found persuasive. Therefore, the rejection of claims 1, 4, 5, 13-15, 18, 19, 27-36, and 38-40 under 35 USC § 112, first paragraph for the reasons set forth in the previous Office Action mailed November 9, 2001 (Paper No. 10) is maintained.

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 1, 4, 5, 13-15, 18, 19, 27-36, and 38-40 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for the reasons set forth in the previous Office Action mailed November 9, 2001 (Paper No. 10).

Claims 1, 4, 5, 13-15, 18, 19, 27-36, and 38-40 are vague and indefinite because claim 1 and 15, respectively, recite the phrases "a method for determining whether an individual is likely to have gastrointestinal cancer" or "a method for determining whether a patient who has been treated for primary breast cancer is likely to have metastatic breast cancer". Applicants have traversed this ground of rejection in Paper No. 16, but

Applicants arguments have not addressed the issue at hand, namely whether or not the claims clearly and particularly delineate the subject matter that Applicants regard as their invention. For example, as stated in the previous Office Action, recitation of the cited phrases renders the claims indefinite because it is unclear whether Applicants consider their invention to be a method for determining whether an individual will develop gastrointestinal or metastatic breast cancer, i.e., a method for assessing an individual's risk for developing gastrointestinal or metastatic breast cancer, or a method for determining that an individual has gastrointestinal or metastatic breast cancer, i.e., a method for diagnosing gastrointestinal or metastatic breast cancer.

Claims 1, 4, 5, 13-15, 18, 19, 27-36, and 38-40 are vague and indefinite because claims 1 and 15 recite the phrase "a parameter *representing* the total concentration of TIMP-1" (italics added for emphasis). Applicants have traversed this ground of rejection, suggesting that deletion of "first" has rendered the ground of rejection moot, but Applicants have not addressed the issue at hand, namely that it is unclear how the parameter "represents" the total concentration of TIMP-1.

Claims 1, 4, 5, 13-15, 18, 19, 27-36, and 38-40 are vague and indefinite because the term "high" in claims 1 and 15 is a relative term that renders the claims indefinite. Applicants have traversed the ground of rejection, suggesting that the specification would enable the practitioner to select the threshold value used to discriminate an affected individual and an unaffected individual with the pre-determined degrees of specificity and sensitivity that the practitioner finds desirable. However, the specification does not disclose the relationship between the degree of the likeliness that an individual has or does not have cancer and the degrees of specificity and sensitivity, so the specification fails to provide a standard for ascertaining the degree of specificity and sensitivity that would need be selected to use the method to determine with a high degree of likelihood that an individual has or does not have cancer. Again, "high" is a relative term. Since the claims require the method to be used to determine whether or not an individual has a high probability of having cancer and the claims do not recite the values of the degrees of specificity and sensitivity that would necessarily be used to

achieve this objective, the degree of the likeliness that an individual has or does not have cancer to which the claims refer cannot be determined.

Claims 1, 4, 5, 13-15, 18, 19, 27-36, and 38-40 are vague and indefinite because claims 1 and 15 recite the phrase "a discriminating value". Applicants have amended claims 1 and 15 to recite, "said discriminating value which identifies the [...] cancer population" and "the discriminating value being a value which has been determined by measuring said parameter in both a healthy control population and a population with known [...] cancer". The claims do not specifically recite how the claim requires the discriminating value to be determined by measuring the total concentration of TIMP-1 in body fluid samples of populations of individuals known to be healthy or to have cancer. Therefore, the present claims are still indefinite. In addition, the "discriminating value" is necessarily the value of the TIMP-1 concentration that discriminates an individual having or likely to have cancer and an individual not having or unlikely to have cancer, but according to the present claims, depending upon the pre-selected variables of specificity and sensitivity, it evident that the discriminating value can vary. Therefore, it is still unclear what discriminatory value must be used discriminate an individual having or likely to have cancer and an individual not having or unlikely to have cancer.

Claims 1, 4, 5, 13-15, 18, 19, 27-36, and 38-40 are vague and indefinite because claims 1 and 15 recite the phrase "a predetermined specificity and/or a predetermined sensitivity". As stated in the previous Office Action, it is unclear how the claim requires the specificity and sensitivity to be predetermined. While the specificity and sensitivity might be arbitrarily determined by the practitioner depending upon "how much loss in specificity is tolerable" (Paper No. 16, page 8, paragraph 1), since the term "high" renders the claims indefinite for the reasons reiterated above, it cannot be ascertained what values of specificity and selectivity need be predetermined in order to discriminate an individual having a *high* likelihood of having cancer and the individual unlikely to have cancer. As the predetermined values of specificity and sensitivity can vary at the discretion of the practitioner, the metes and bounds of the invention are not clearly delineated by the claims.

New Grounds of Claim Rej ctions

Claim Rejections –35 USC § 112

11. Claims 1, 4, 5, 13-15, 18, 19, 27-36, and 38-40 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1 and 15 recite a limitation requiring the body fluid sample of said individual to be "other than blood serum". However, there does not appear to be proper and sufficient antecedent basis in the specification for recitation of this limitation in the claims. Therefore, the limitation appears to constitute new matter and accordingly recitation of the limitation in claims 1 and 15 appears to violate the written description requirement set forth under 35 USC § 112, first paragraph. This issue might be resolved if Applicants were to point to specific disclosures in the specification that are believed to provide support for recitation of the limitation in the claims.

12. Claims 1, 4, 5, 13-15, 18, 19, 27-36, and 38-40 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 4, 5, 13-15, 18, 19, 27-36, and 38-40 are indefinite because claims 1 and 15 recite the positive process step, "whereby the **likelihood** that said individual is **likely** to have [...] cancer is determined" (emphasis added) and the preambles of the claims recite "[a] method for determining whether an individual is likely to have [...] cancer". The positive process steps of claims 1 and 15 not clearly relate back to the preambles of the claims and moreover, the objectives of practicing the claimed method, which are recited in the preambles of the claims, are incongruous with those recited in the positive process steps. To meet the objectives set forth in the positive process steps of the claims, the practitioner would have to determine the likelihood of the likelihood that an individual has or will have cancer. Amending claim 1, for example, to

recite "whereby the likelihood that said individual has or will have gastrointestinal cancer is determined" can obviate the ground of this rejection.

Conclusion

13. No claims are allowed.

14. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

15. This application contains claims 6-12 and 20-26 drawn to an invention non-elected with traverse in Paper No. 7. A complete reply to the final rejection must include cancellation of non-elected claims or other appropriate action (37 CFR § 1.144). See MPEP § 821.01.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen L. Rawlings, Ph.D. whose telephone number is (703) 305-3008. The examiner can normally be reached on Monday-Thursday, alternate Fridays, 8:00AM-5:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony C. Caputa, Ph.D. can be reached on (703) 308-3995. The fax

phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Stephen L. Rawlings, Ph.D.
Examiner
Art Unit 1642

slr
July 1, 2002

ANTHONY C. CAPUTA
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600